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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/235,153	01/22/1999	WILFRED A. KELLER	SB-B750	5109

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EXAMINER
EINSMANN, JULIET CAROLINE

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1634	23

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/235,153	Applicant(s) KELLER ET AL.	
	Examiner Juliet Einsmann	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-38,40-46 and 48-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-38,40-46 and 48-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 January 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/18/02 has been entered.

2. This action is written in response applicant's correspondence submitted 3/18/02 and 5/16/02, paper numbers 19 and 22. Claims 34, 40, 49-66 have been amended, claims 67-80 have been added, and claims 39 and 47 have been canceled. Claims 34-38, 40-46, and 48-80 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Drawings

3. The drawings are approved for examination.

Claim Rejections - 35 USC § 112

4. Claims 34-38, 40-46, and 77-80 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In the instantly rejected claims, the new limitation of "with the proviso that said plant is not rice or *Arabidopsis*" in claims 34, 40, and 49, appears to represent new matter. Applicant identified page 18, line 16 to page 19, line 21 as basis for this exclusionary proviso. However, a careful review of this section of the specification did not result in the identification of basis for this specific negative proviso. This section of the specification merely discusses generally modifying secondary metabolites in the phenylpropanoid metabolic pathway. There is no mention in this section of any particular plant species, let alone of the particular exclusion rice and *Arabidopsis*. As noted by MPEP 2173.05(i),

> "Any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli , 231 USPQ 393 (Bd. App. 1983) aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement."

Since no basis has been identified, the claims are rejected as incorporating new matter. The remaining rejected claims depend from these three independent claims, and thus they are rejected for incorporating the same new matter.

5. Claims 34-38, 40-46, and 48-80 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first

paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In the instantly rejected claims, the new limitation of "non-native to said secondary metabolic pathway" or "non-native to said phenylpropanoid pathway" or in claims 34, 49, 67, and 72 appears to represent new matter. This rejection applies to these amendments wherein "non-native" has some definition other than "heterologous." Applicant indicates that support for this amendment is found in cancelled claim 39 that recites a "heterologous" enzyme, thus implying that a protein that is "non-native" to said secondary metabolic pathway is "heterologous" to that pathway. A "heterologous gene" is understood to be "any gene that is isolated from organism A and transferred into organism B" (Dictionary of Gene Technology, 1995, p. 210). However, Applicant's arguments seem to be implying that a protein that is "non-native" to the pathway is some narrower definition wherein the protein must not be active in the same metabolic pathway in another plant, for example. That is, applicant appears to be arguing that "non-native to the pathway" is narrower than "heterologous," but this is not clear from the specification. No specific basis for this definition was identified in applicant's paper, nor did a review of the specification by the examiner find any basis for the limitation. It is this narrower definition of "non-native" that is not supported by the specification. As noted by MPEP 2173.05(i),

> "Any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli , 231 USPQ 393 (Bd. App. 1983) aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement."

Since no basis has been identified, the claims are rejected as incorporating new matter.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 34-38, 40-46, and 48-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 34-38, 40-46, and 48-80 are indefinite over the recitation "said protein being non-native to said secondary metabolic pathway" because it is not clear what it means for the protein to be "non-native" to said secondary metabolic pathway. Applicant indicates that support for this amendment is found in cancelled claim 39 that recites a "heterologous" enzyme, thus implying that a protein that is "non-native" to said secondary metabolic pathway is "heterologous" to that pathway. A "heterologous gene" is understood to be "any gene that is isolated from organism A and transferred into organism B" (Dictionary of Gene Technology, 1995, p. 210). However, Applicant's arguments seem to be implying that a protein that is "non-native" to the pathway is some narrower definition wherein the protein must not be active in the same metabolic pathway in another plant, for example. That is, applicant appears to be arguing that "non-native to the pathway" is narrower than "heterologous," but this is not clear from the specification. Thus, the meaning of this phrase in the claims is unclear.

Claim 62 is indefinite over the recitation "Brassicaceae (=Cruciferae)" because it is unclear if applicant is intending that the plant be a member of the family Brassicaceae or the family Cruciferae. The claim appears to be implying that these two families are identical, but this is repugnant to the meaning of these families in the art. For example, the Hortiplex Plant

Database provides a list of the genera included in both species. While the family Cruciferae has 105 genera included therein, the family Brassicaceae has only seven, none of which are overlapping (see web site print outs enclosed to herein). Thus, the subject matter encompassed by claim 62 is unclear. The claims have been treated herein as if they require the plant to be a member of the family Cruciferae, of which the genus Brassica is a member.

Claim Rejections - 35 USC § 102

8. Claims 34-37, 44, 48, 67 and 72 rejected under 35 U.S.C. 102(e) as being anticipated by Cheng *et al.* (US 5948667).

Cheng *et al.* teach a method for altering the nutritional profile of a plant, comprising the steps of:

selecting a nucleic acid sequence for it's ability to encode a protein capable of modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile in a plant;

transforming a plant cell with an expression cassette comprising said nucleic acid sequence;

recovering a genetically altered plant from said plant cell, said genetically altered plant characterized by an altered nutritional profile relative to a wild-type of said plant (Col. 17, line 56-Col. 19, line 25).

The methods taught by Cheng *et al.* comprise the transformation of *B. napus* with an expression vector comprising a seed specific promoter (the oleosin promoter) and a coding sequence for xylanase. The transformation of the plant with a coding sequence xylanase results

in the production of transgenic plants with altered nutritional profiles because they contain a higher level of xylanse than wild type plants.

9. Claims 34-36, 44, 46, 48, 67, 72, and 77-79 are rejected under 35 U.S.C. 102(b) as being anticipated by Chapple *et al.* (WO 97/23599), and claims 40, 48, 49-51, 54, 58, 59, 60, 61, 62, 63, 64, 65, 66, and 77-80 are rejected under 35 U.S.C. 102(a) as being anticipated by Chapple *et al.* (WO 97/23599).

This application is a CIP of US 09/012453, now abandoned. The '453 application provides methods for modifying the phenolic compounds of plants by transforming the plants with genes that will act upon a product within the phenylpropanoid pathway. This disclosure is not sufficient to support the breadth of at least claims 34-36, 44, 46, and 48 since these claims encompass the use of any nucleic acid sequence which encodes a protein capable of modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of a plant, not only the phenylpropanoid pathway. Thus, Chapple *et al.* is a 102(b) reference against some claims and a 102(a) reference against other claims.

Chapple *et al.* teach a method for altering the nutritional profile of a plant, comprising the steps of:

selecting a nucleic acid sequence for it's ability to encode a protein capable of modifying the utilization of a substrate in the phenylpropanoid pathway of said plant, said protein being non-native to said secondary metabolic pathway;

transforming a plant cell with an expression cassette comprising said nucleic acid sequence;

recovering a genetically altered plant from said plant cell, said genetically altered plant characterized by an altered nutritional profile relative to a wild-type of said plant (Example 5).

Chapple *et al.* teach the transformation of plants with the F5H gene in order to alter the lignin content in plants. Chapple *et al.* exemplify this method in the transformation of Arabidopsis thaliana (a crucifer) and further teach that this method is useful to transform other plants such as alfalfa, rice, maize and oil seed rape (Brassica) (p. 7, lines 15-20). Chapple *et al.* teach the growth of such plants to permit the formation of seed, and the recovery of said seed (p. 19, lines 4-5). Chapple *et al.* teach the use of tissue specific promoters (p. 15, lines 25-29). Chapple *et al.* teach method steps in which at least one genetically altered plant having altered lignin content is identified (p. 24 line 25-p. 24 line 7, Tables 1 and 2). Since the F5H gene effects the production of a product in the phenylpropanoid pathway which is necessary for the production of sinapine, (i.e. 5-hydroxyferulic acid) plants with decreased F5H activity as taught by Chapple *et al.* would inherently have the property of decreased sinapine levels compared to the wild type plants.

10. Claims 34, 35, 36, 40, 46 , 48, 49, 50, 51, 54, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 72, and 77-80 are rejected under 35 U.S.C. 102(b) as being anticipated by Van Doorsselaere *et al.* (WO 93/05160).

Van Doorsselaere *et al.* teach a method for altering the nutritional profile of a plant, comprising the steps of:

selecting a nucleic acid sequence for it's ability to encode a protein capable of modifying the utilization of a substrate in the phenylpropanoid pathway of said plant, said protein being non-native to said secondary metabolic pathway;

transforming a plant cell with an expression cassette comprising said nucleic acid sequence;

recovering a genetically altered plant from said plant cell, said genetically altered plant characterized by an altered nutritional profile relative to a wild-type of said plant (Example 4).

Van Doorsselaere *et al.* teach the transformation of plants with a nucleic acid encoding O-methyl transferase (OMT) in order to alter the lignin content in plants. Van Doorsselaere *et al.* exemplify this method in the transformation of poplar trees and further teach that this method is useful to transform other plants such as alfalfa, rice, maize and oil seed rape (Brassica) (p. 13, lines 15-26). Van Doorsselaere *et al.* teach the use of tissue specific promoters (p. 12, lines 15-20). Van Doorsselaere *et al.* teach method steps in which at least one genetically altered plant having altered lignin content is identified (p. 21 -23). Since the OMT gene effects the production of a product in the phenylpropanoid pathway which is necessary for the production of sinapine, (i.e. ferulic acid) plants with decreased OMT activity as taught by Van Doorsselaere *et al.* would inherently have the property of decreased sinapine levels compared to the wild type plants.

Claim Rejections - 35 USC § 103

11. Claims 34-36, 40-42, 44, 48, 49, 50, 54, 55, 56, 58, 59, 60, 61, 62, 63, 66, 67, 68, 69, 72, 73, 74, 77, 78, 79, and 80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murata in view of Londesborough *et al.* (WO 96/00789).

Murata teaches a method of making a genetically transformed plant comprising:

selecting a nucleic acid sequence for it's ability to encode a protein capable of modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of a plant, said plant protein being non-native to said secondary metabolic pathway;

transforming a plant cell with an expression cassette comprising said nucleic acid sequence;

recovering a genetically altered plant from said plant cell, said genetically altered plant characterized by an altered nutritional profile relative to a wild-type of said plant (see Examples 8 (page 8) and 14 (page 10)).

The methods taught by Murata are specifically directed for the purpose of producing osmo-tolerant plants, however, these methods necessarily meet the limitations of the instant claims. Murata specifically selects a gene encoding choline oxidase for plant transformation, selecting the choline oxidase for it's ability to encode choline oxidase, a protein capable of modifying the utilization of a substrate in a secondary metabolic pathway. Thus, Murata has selected a nucleic acid sequence for it's ability to encode a protein capable of modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of a plant. The transgenic plants recovered by Murata inherently have an altered nutritional profile by virtue of the fact that they are expressing choline oxidase. These plants would have lower lignin and sinapine content.

Murata further grows the plant obtained under conditions which permit the formation of a seed (page 10, line 10, for example). Murata teaches the plants and seeds produced by the plants obtained by this method (page 10, line 10-15), these seeds inherently have reduced lignin and sinapine content.

Murata exemplifies the use of this method to produce transgenic Arabidopsis thaliana, of the family cruciferae, (example 8) and rice, Oryza sativa- family gramineacae (example 10). Murata does not teach methods wherein the plant is not rice or Arabidopsis. However, Murata

teaches that "The range of plants to which can be conferred salt tolerance and/or osmotolerance by the method of this invention is very wide (p. 5, lines 29-30)."

Londesborough *et al.* teach methods for the production of osmotolerant plants, and particularly recite a number of different plant species that it would be desirable to produce osmotolerant versions of, including such plants as oilseed rape (a member of the genus Brassica), corn (a member of the family gramineae), sunflower (a member of the family compositae), and soybean (also known as Glycine max, a member of the family leguminosae) (see p. 18, lines 3-12).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have made transgenic plants of any of a variety of species using the methodology provided by Murata. The ordinary practitioner would have been motivated to utilize the methodology of Murata on other plant species in order to have provided drought tolerant plants, as Murata particularly teaches that a wide variety of plants can be conferred salt tolerance and/or osmotolerance, and Londesborough *et al.* particularly teach that this property would be of benefit for a wide range of plants.

12. Claims 34-38, 40-42, 44, 46, 49-56, 58-60, 63, 66, 78, 79, and 80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murata in view of Willmitzer *et al.* (WO 92/01042).

Murata teaches a method of making a genetically transformed plant comprising:

selecting a nucleic acid sequence for it's ability to encode a protein capable of modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of a plant, said plant protein being non-native to said secondary metabolic pathway;

transforming a plant cell with an expression cassette comprising said nucleic acid sequence;

recovering a genetically altered plant from said plant cell, said genetically altered plant characterized by an altered nutritional profile relative to a wild-type of said plant (see Examples 8 (page 8) and 14 (page 10)).

The methods taught by Murata are specifically directed for the purpose of producing osmo-tolerant plants, however, these methods necessarily meet the limitations of the instant claims. Murata specifically selects a gene encoding choline oxidase for plant transformation, selecting the choline oxidase for it's ability to encode choline oxidase, a protein capable of modifying the utilization of a substrate in a secondary metabolic pathway. Thus, Murata has selected a nucleic acid sequence for it's ability to encode a protein capable of modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of a plant. The transgenic plants recovered by Murata inherently have an altered nutritional profile by virtue of the fact that they are expressing choline oxidase. These plants would have lower lignin and sinapine content.

Murata further grows the plant obtained under conditions which permit the formation of a seed (page 10, line 10, for example). Murata teaches the plants and seeds produced by the plants obtained by this method (page 10, line 10-15), these seeds inherently have reduced lignin and sinapine content.

Murata exemplifies the use of this method to produce transgenic Arabidopsis thaliana, of the family cruciferae, (example 8) and rice, Oryza sativa- family gramineacae (example 10).

Murata further teaches that choline oxidase is an enzyme which is commercially available (p. 2, lines 55-56).

Murata does not teach methods in which the promoter is tissue selective, or specifically seed selective, and Murata does not teach plants that are not rice or Arabodipsis.

Willmitzer *et al.* teach transgenic plants expressing industrial enzymes, and methods for the production of such plants. The industrial enzymes suggested by Willmitzer *et al.* for use in these methods include oxidoreductases (p. 6, line 22). They teach that the DNA sequence encoding the enzyme of interest under the control of a promoter such as a seed specific promoter such as the phaseolin promoter (p. 4, lines 27-31). Willmitzer *et al.* teach a variety of plants useful for the introduction of the enzyme, including tobacco, potato, tomato, pea, soy, and cereals (p. 7, lines 19-21), and further teach that either the entire plant or parts thereof may be useful for animal feeds (p. 7, lines10-13). Willmitzer *et al.* teach vectors for the integration of foreign DNA into plant cells and the introduction of these vectors into Agrobacterium species (p. 9, line 28-p. 9, line 19).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used seed specific promoters for the expression of choline oxidase in plants as taught by Willmitzer *et al.* The ordinary practitioner would have been motivated to do so by the fact that choline oxidase is an enzyme which is sold commercially and because Willmitzer *et al.* expressly teach that the production of enzymes in plants overcomes two major obstacles in industrial enzyme production, "Firstly, higher plants have biosynthetic capacity to perform the requisite post-translational modifications occurring in eukayrotic cells of mammalian or other origin. Secondly, transgenic plants grown in the field need very little extra

energy for growth (and hence for the production of proteins such as industrial enzymes) and furthermore do not give rise to any major problems with respect to waste management (p. 4, lines 10-18)." Furthermore, Murata provides the nucleic acid sequence encoding choline oxidase and demonstrates that it can be successfully expressed in transgenic plants. Willmitzer *et al.* provide the necessary suggestion and direction to motivate the production of choline oxidases in plants, and thus, in the absence secondary considerations such as unexpected results, the claimed invention is obvious over the prior art.

13. Claims 38 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chapple *et al.* (WO 97/23599) in view of both Kennley (WO 5662958) and Willmitzer *et al.* (WO 92/01042).

Chapple *et al.* teach a method for altering the nutritional profile of a plant, comprising the steps of:

selecting a nucleic acid sequence for it's ability to encode a protein capable of modifying the utilization of a substrate in the phenylpropanoid pathway of said plant;

transforming a plant cell with an expression cassette comprising said nucleic acid sequence;

recovering a genetically altered plant from said plant cell, said genetically altered plant characterized by an altered nutritional profile relative to a wild-type of said plant (Example 5).

Chapple *et al.* teach the transformation of plants with the F5H gene in order to alter the lignin content in plants. Chapple *et al.* exemplify this method in the transformation of Arabidopsis thaliana (a crucifer) and further teach that this method is useful to transform other plants such as alfalfa, rice, maize and oil seed rape (Brassica) (p. 7, lines 15-20). Chapple *et al.*

teach the growth of such plants to permit the formation of seed, and the recovery of said seed (p. 19, lines 4-5). Chapple *et al.* teach the use of tissue specific promoters (p. 15, lines 25-29). Chapple *et al.* teach method steps in which at least one genetically altered plant having altered lignin content is identified (p. 24 line 25-p. 24 line 7, Tables 1 and 2). Since the F5H gene effects the production of a product in the phenylpropanoid pathway which is necessary for the production of sinapine, (i.e. 5-hydroxyferulic acid) plants with decreased F5H activity as taught by Chapple *et al.* would inherently have the property of decreased sinapine levels compared to the wild type plants.

Chapple *et al.* do not teach methods in which a seed selective promoter is used to direct the expression of the nucleic acid sequence to seeds.

At the time the invention was made, it was routine to use the seeds of cruciferous plants as animal feed. Furthermore, it was widely known that the lignin content in such seeds is an anti-nutritional factor. For example, Kennley *et al.* teach that lignin within canola seed prevents extensive degradation of cellulose and hemicellulose by cellulolytic microorganisms (Col. 3, lines 30-40).

Willmitzer *et al.* provide methods for the transformation of plants with heterologous polypeptides, and specifically teach methodology for the direction of such heterologous polypeptides to the seeds of such plants. They teach that the DNA sequence encoding the enzyme of interest under the control of a promoter such as a seed specific promoter such as the phaseolin promoter (p. 4, lines 27-31).

Therefore, It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used seed specific promoters such as those provided by

Willmitzer *et al.* in the methods taught by Chapple *et al.* The ordinary practitioner would have been motivated to produce such plants in order to provide canola seed (Brassica napus) which has reduced lignin content, since Kennley *et al.* teach that "lignin within the canola seed coat prevent extensive degradation of cellulose and hemicellulose by cellulolytic microorganisms in the rumen or by the acidic environment of the abomasum and the small intestine. Some method of treatment is required to alter the seed to a form suitable for utilization by ruminants (Col. 3, lines 33-37)." Thus, in light of the teachings provided in the prior art, the instant invention is obvious to one of ordinary skill in the art at the time the invention was made.

14. Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Van Doorsselaere *et al.* in view of Chapple *et al.* (The Plant Cell, Vol. 4, 1413-1424).

Van Doorsselaere *et al.* teach a method for altering the nutritional profile of a plant, comprising the steps of:

selecting a nucleic acid sequence for it's ability to encode a protein capable of modifying the utilization of a substrate in the phenylpropanoid pathway of said plant;

transforming a plant cell with an expression cassette comprising said nucleic acid sequence;

recovering a genetically altered plant from said plant cell, said genetically altered plant characterized by an altered nutritional profile relative to a wild-type of said plant (Example 4).

Van Doorsselaere *et al.* teach the transformation of plants with a nucleic acid encoding O-methyl transferase (OMT) in order to alter the lignin content in plants. Van Doorsselaere *et al.* exemplify this method in the transformation of poplar trees and further teach that this method is useful to transform other plants such as alfalfa, rice, maize and oil seed rape (Brassica) (p. 13,

lines 15-26). Van Doorsselaere *et al.* teach the use of tissue specific promoters (p. 12, lines 15-20). Van Doorsselaere *et al.* teach method steps in which at least one genetically altered plant having altered lignin content is identified (p. 21 -23). Since the OMT gene effects the production of a product in the phenylpropanoid pathway which is necessary for the production of sinapine, (i.e. ferulic acid) plants with decreased OMT activity as taught by Van Doorsselaere *et al.* would inherently have the property of decreased sinapine levels compared to the wild type plants.

Van Doorsselaere *et al.* do not teach a method in which the transgenic plants are assayed for sinapine content.

Chapple *et al.* teach the scheme for the phenylpropanoid pathway (Figure 1). OMT is an enzyme which is necessary for the production of sinapoyl choline, in addition to being necessary for the production of lignin. Chapple *et al.* further teach methods for analysis of sinapine (sinapoyl choline) in seeds (p. 1421-1422). Chapple *et al.* teach that the presence of high levels of sinapine in canola seeds has a negative impact on the value of canola meal, and that it should also be possible to genetically eliminate sinapoyl choline from Brassica seeds without a deleterious effect on seedling growth.

Thus, in light of the transgenic plants provided by Van Doorsselaere *et al.* and the teachings taught by Chapple *et al.*, It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included an assay to detect a transgenic plant with reduced sinapine content in the methods taught by Van Doorsselaere *et al.* The ordinary practitioner would have been motivated by the teachings of Chapple *et al.* that such a plant should be possible to produce by genetic modification and the fact that Van Doorsselaere *et al.* provide transgenic plants that have a disruption in the pathway that leads to the production

of sinapoyl choline. For these reasons, the claimed invention is considered *prima facie* obvious in view of the prior art.

RESPONSE TO REMARKS

Applicant's remarks are addressed insofar as they are relevant to the rejections of the instantly pending claims.

Applicant's remarks concerning Cheng *et al.* have been carefully considered, and are not persuasive. Applicant argues that hemicellulose is a final product found in plant primary and secondary cell walls, thus implying that hemicellulose is not a substrate in plant secondary metabolic pathways. However, hemicellulose is also a substrate in plant secondary metabolic pathways which involve the metabolism (i.e. via hydrolysis or other degradation or modification) of hemicellulose in plant pathways. Thus, while it may be a final product in the pathway that leads to hemicellulose, it is also a substrate in further secondary pathways. Furthermore, applicant argues that Cheng's methods are inapposite with the present invention because Cheng *et al.* transform the xylanase and render it unavailable. This is not persuasive. The method taught by Cheng *et al.* meets all of the limitations of the rejected method claims, as discussed in the rejection. Furthermore, Cheng *et al.*'s specific purpose is to produce nutritionally altered animal feed (see Abstract, for example).

Applicant argues that Chapple *et al.* does not anticipate the instantly claimed invention because the protein introduced by Chapple *et al.* is native to the secondary metabolic pathway of interest. However, this is not persuasive. Applicant's interpretation of "non-native to the secondary metabolic pathway" is narrower than the one being used by the examiner. The examiner understands this limitation to mean that some protein that is not naturally found in the

transgenic plant of interest is being expressed in the transgenic plant. This interpretation is supported by the fact that applicant cites the use of the word "heterologous" as support for the addition of this limitation to the claims. A "heterologous gene" is understood to be "any gene that is isolated from organism A and transferred into organism B" (Dictionary of Gene Technology, 1995, p. 210). Chapple *et al.* specifically teach that their method "relates to the modification of lignin composition in a plant cell by the introduction of a foreign plant gene encoding an active ferulate-5-hydroxylase (F5H) enzyme (p. 1, lines 7-9)." Thus, the enzyme being introduced into the plants is a non-native enzyme, in the sense that it is not the enzyme that is naturally encoded by the transgenic plants, even if it has the same function as an enzyme that may be functional in that pathway. Thus, the rejection over Chapple *et al.* is maintained.

Applicant argues that Van Doorsselaere *et al.* teach the transformation of plants with an OMT sequence that is native to the lignin biosynthetic pathway. This argument is not persuasive for the same reasons that it was not persuasive concerning the teachings of Chapple *et al.* is teaching the transformation of plants, exemplified in poplar, with tobacco OMT. Thus, the OMT being expressed in the transformed plants taught by Chapple *et al.* is not native to the transgenic plants being produced nor to the secondary metabolic pathways of the plants being produced by the methods taught by Chapple *et al.* Applicant further argues that Van Doorsselaere *et al.* do not provide "enabling details" as to how the transformation of plants other than poplar would be accomplished, however, Applicant does not provide any reasons or evidence that the teachings and methodology provided by Van Doorsselaere *et al.* are non-enabling, since they provide methodology for plant transformation, constructs for plant transformation, and a specific teaching that the constructs provided in their specification may be used to transform other

species as listed (p. 12-13). Arguments of counsel are not found to be persuasive in the absence of a factual showing. MPEP 716.01(c) makes clear that

> "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant."

Applicant argues that Murata *et al.* are not concerned with altering the nutritional profile of the plant. However, as previously stated, the alteration of the nutritional profile of the plant when transforming it with a gene encoding choline oxidase is a necessary effect of such a transformation. Murata *et al.* completes such a transformation, and thus changes the nutritional profile of a plant whether they were aware of this feature of their method or not. Applicant further argues that Willmitzer *et al.* are very clear that it is not their purpose to change the physical characteristics of the plant itself, citing language from Willmitzer *et al.* that notes that their invention comprises transgenic plants transformed with nucleic acids encoding enzymes "with the exception of enzymes conferring improved growth properties or desirable physical characteristics to living plants producing them." However, Willmitzer *et al.* further state that "the enzyme will typically not confer improved growth properties (e.g. increased resistance against pests or pathogens), a higher content of nutrients (by means of an altered amino acid composition) or desirable physical characteristics (i.e. reduced viscosity of fruit products) to a plant (***if it does, this will be incidental to the true purpose which is to synthesize the enzyme***) (emphasis added) (p. 3, lines 14-21)." Thus, Willmitzer *et al.* are not teaching away from plants with desirable physical characteristics, they are simply not transforming plants with these effects

as the goal. Applicant is reminded that MPEP 2123 teaches that "A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments." Thus, simply because Willmitzer *et al.* have a different purpose than applicant, does not mean that they teach away from the instantly claimed invention. The rejection is quite clear in providing that the motivation for production of transgenic plants expressing a heterologous nucleic acid that encodes choline oxidase is to provide a means for the production of this industrially useful enzyme. Thus, the examiner concludes that Willmitzer *et al.* do not teach away from the claimed invention, and the rejection of record is maintained.

Applicant's arguments concerning the rejection of claims 38 and 52 in view of Chapple *et al.*, Kennley *et al.*, and Willmitzer *et al.* are duplicative of those that have been previously addressed.

Applicant's arguments concerning the rejections of Van Doorsselaere *et al.* in view of Chapple *et al.* are a piecemeal analysis focusing on the deficiencies of the Van Doorsselaere *et al.* reference. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant's concerns with regard to Van Doorsselaere *et al.* have been previously addressed.

Finally on page 15, Applicant's traverse the assertion that the methods of Murata *et al.* inherently meet the method steps of the claims of record. Applicant asserts that Murata *et al.* do not select a nucleic acid for its ability to encode a protein capable of modifying utilization of a substrate in a secondary metabolic pathway associated with the nutritional profile of a plant.

However, Murata *et al.* specifically select a nucleic acid encoding choline oxidase for transformation of the plant, selecting a nucleic acid encoding choline oxidase for its ability to encode a protein capable of modifying choline, which is inherently a substrate in a secondary metabolic pathway associated with the nutritional profile of a plant. Thus, Murata *et al.* do in fact meet this positive selection step.

New rejections have been added to address the amendments to the claims.

Allowable Subject Matter

15. Claims 43 and 52 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

16. While the prior art teaches methods for producing transgenic plants expressing heterologous choline oxidase (Murata, for example) and different transgenic plants expressing betaine aldehyde dehydrogenase (Holmström *et al.*, for example), the prior art does not teach or suggest methods in which both choline oxidase and betaine aldehyde dehydrogenase are introduced into the same plant under the control of a seed specific promoter.

Conclusion

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Juliet C Einsmann
Examiner
Art Unit 1655

June 20, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600